P3-163 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Gefitinib versus chemotherapy as first-line treatment in elder patients with advanced non-small-cell lung cancer

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Background: Elder patients with non-small cell lung cancer (NSCLC) have been habitually underrepresented in clinical trails. Retrospective analysis have shown similar therapeutic outcome of platinum-based combined chemotherapy for fit elderly, albeit more toxicity compared with younger counterparts. Gefitinib, an oral EGFR-TKI was generally well tolerated with clinically meaningful anti-tumor activity in previously treated patients as well as chemo-naïve patients. The aim of the study was to retrospectively evaluate the toxicity, efficacy and survival of gefitinib versus platinum-based combined chemotherapy as first-line treatment for a series of Chinese patients aged 70 and over with advanced NSCLC.

Methods: from January 2002 to December 2005, 38 patients received chemotherapy (17 of Novelbine, 8 of Gemcitabine, 7 of taxol and 7 of taxotere, all of which combined with cisplatin or carboplatin) and 17 patients received gefitinib 250mg once daily as first line treatment.

Results: Of the 38 patients who received chemotherapy, the median age was 73.3 years old (70-80) with 68.4% male, 73.7% adenocarcinoma and 78.9% patients were in stage 4. The PS of all patients was 0-1. Of the 17 patients who received gefitinib, the median age was 76.9 years old (70-85) with 58.8% male, 64.7% adenocarcinoma and 82.4% patients were in stage 4. The PS of 6 patients was over 2. The most frequently reported adverse events for chemotherapy group were neutropenia (92.1%) and thrombocytopenia(73.7%). Grade 3/4 neutropenia was 21.1% and four patients had nertropenia febril. Grade 3/4 thrombocytopenia was 10.5% and 2 patients need blood transfusion. Other grade 3/4 adverse effects included 3 cases of vomiting and one case of cardiac arrhythmia. 4 patients withdrew the chemotherapy due to side effects. The most frequently reported adverse events for gefitinib group were skin disorders (70.6%) and diarrhea (35.3%). The majority of these events were mild with grade 1 to grade 2. One patient was hospitalization due to grade 3 diarrhea and recovered without drug administration disruption. Other adverse events included 2 cases of nausea, 1 case of oral ulcer and 1 case of elevation in hepatic enzymes. No patient withdrew due to adverse effect. The partial response and disease control rate were 21.1% and 78.9% for chemotherapy group versus 17.6% and 68.8% for gefitinib group. The median progress free survival and overall survival time were 4.93 ± 0.747 months (95% CI: 3.465, 7.395) and 13.882 ± 0.718 months (95% CI: 12.892, 20.708) for chemotherapy group versus 6.4 ± 1.852 months (95%CI: 2.770, 10.030) and 15.882 ± 2.029 months (95%CI: 13.654, 20.505). The one-year survival was 52.6% in chemotherapy group versus 47.1% in gefitinib group. There is no statistical significance between the two groups for efficacy, progress free survival time and overall survival time.

Conclusion: Platinum-based combined chemotherapy was well tolerated and provides significant anti-tumor activity in elder patients. Gefitinib as first-line treatment provides similar clinical benefit with less toxicity for the elder NSCLC patients.

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A phase II trial of pemetrexed(p) in patients (pts) with performance status (PS) 2 and 3 as 1st- and 2nd- line treatment for advanced non-small-cell lung cancer (NSCLC)

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P (Alimta) is approved as 2nd-line therapy in pts with advanced NSCLC. In a phase III trial comparing P with docetaxel (D), median survival was 8.3 mos (P) vs 7.9 mos (D); P had a more favorable safety profile than D (Hanna, 2004). There are few data on pts with PS 3, and ASCO 2003 guidelines recommend that chemotherapy be reserved for pts with PS 0, 1 and possibly 2. Since P is well tolerated, PS3 pts may tolerate and benefit from it. In this trial, we treated 20 pts with stage IIIb/IV NSCLC and PS 2 or 3, who were chemo-naive or had received 1 prior regimen. Pts received P 500mg/m^2 IV D1 Q 3 wks. All pts received folic acid, vitamin B12 and dexamethasone prophylaxis. Serial blood samples were obtained to monitor inflammatory cytokines, and symptoms were monitored using the validated MDASI instrument. All pts were assessable for toxicity-symptoms, and 17 pts were evaluable for response (assessed after 1st cycle). Pt characteristics: 8 pts were PS 3 (4/8 1st line) and 12 pts were PS 2 (6/12 1st line). Median age was 69 for PS3 and 68 for PS2. 5/8 PS3 pts and 6/12 PS2 pts were men. 2/8 PS3 pts and 4/12 PS2 pts had stage IIIb. 4/8 PS3 pts and 6/12 PS2 pts were chemo-naïve. Grade 3-4 toxicities for PS3/PS2 cohorts were: neutropenia 0/1 pt, anemia 1/2, fatigue 2/0, pneumonia 1/1, hypotension 1/1, neutropenic fever 0/1, atrial fibrillation 1/1. Response rates (RR) in PS3 pts were minor response (MR) 1/8, stable disease (SD) 5/8, progressive disease (PD) 2/8; RR in PS2 pts were partial response (PR) 1/12, MR 2/12, SD 3/12, PD 3/12, inevaluable 3/12. RR by line of therapy: 1st line 6/10 SD, 2/10 PD, 2/10 inevaluable, and 2nd line, 1/10 PR, 2/10 MR, 3/10 SD, 3/10 PD, and 1/10 inevaluable. Reasons for PS3 pts coming off study were progression (4/8), constitutional toxicity (3/8), fatal pulmonary emboli (1/8); PS2 pts came off study due to progression (5/12), constitutional toxicity (2/12), and pneumonia (1/12). 4/12 PS2 pts are still on study. These preliminary data suggest that single-agent P is well-tolerated and has a promising RR in poor PS pts. Total planned accrual is 30 PS3 and 45 PS2 pts. Survival, symptom, and cytokine data will be presented.

NSCLC: Radiation

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Utility of SPECT for metabolic and functional lung imaging in radiation therapy treatment planning for lung cancer

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Background: Conformal radiotherapy of lung tumors relies on anatomic imaging with CT scan to define both targets and critical structures, but has its drawbacks in differentiating atelectasis from tumor. Also, it may not represent the metabolic tumor volume and functional lung volume. We attempted to evaluate the utility of SPECT to gain information

regarding metabolic tumor volume as well as functional lung volume with the intent to design the beam portal for sparing functional lung.

Patients and Methods: Nine patients of lung cancer suitable for radiotherapy had CT scan, MIBI (Sestamibi) SPECT and MAA (Macro-Aggregated Albumin) SPECT scans with fiducial markers and accurately co-registered using statistical parametric mapping software. These registered images were transferred into the planning system in which MIBI-SPECT images guided the target volume delineation and MAA-SPECT scans were used to define volume of perfused 'functioning' lung. When feasible, the design of the beam portal was placed attempting for a conformal approach. The gross tumor volume (GTV) of CT and MIBI, whole lung (WL) and functional lung (FL) volumes were calculated. The volume of lung receiving more than 20 Gy (V20) and mean lung dose (MLD) for WL and FL were also calculated.

Results: MIBI and perfusion images was co-registered with radiotherapy planning CT scans for delineation of target and functional lung. In comparison to the CT defined target volumes, the MIBI defined target volume were smaller in 4, larger in 1, similar in 2 and no appreciable uptake in 2 patients (these patients had also received prior chemotherapy). Perfusion SPECT revealed the ipsilateral lung completely non functional (same side as tumor) in 3 patients and so the functional lung was spared. In the other 6 patients with perfusion defect in and around the tumor bearing region, an attempt was made for conformal approach to spare the functional lung. (1.ppt)

Conclusion: SPECT images with MIBI and MAA were useful for mapping the metabolic target volume and functional lung. This enables to design beam portals for conformal avoidance of functional lung so as to reduce radiation morbidity.

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Radiation oncologists' attitudes on radiation volume and dose schedule when considering concurrent radiochemotherapy for stage III non-small cell lung cancer: A questionnaire study

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A brief questionnaire was performed before starting a new prospective clinical trial employing concurrent radiochemotherapy (CRCT) for stage III non-small cell lung cancer (NSCLC) in 2005 to survey radiation oncologists' attitudes. A questionnaire consisted of 12 questions, which intended to evaluate career length, personal comfort degree on CRCT, preferred radiation dose schedules, and target volumes both in radiation alone and CRCT settings. This was circulated among 28 candidate radiation oncologists who would participate in the CRCT trial, and 17 responses were collected.

Career lengths were longer than 5 years in six (35.3%), 2~5 years in seven (41.2%), and shorter than 2 years in four (23.5%). All respondents agreed on the efficacy of CRCT, however, 10 (58.8%) were not comfortable with CRCT regimen. There was minor tendency toward more conservative attitudes with respects to fractional dose, doses to primary, gross/elective lymph nodes, and most distal lymphatics to cover, mainly based on concerns of increased side effects, however, none was significant.

Table. Intended radiation therapy details in radiation alone versus concurrent radiochemotherapy settings.

	Setting			
	RT alone		CRCT	
Dose/fraction				
1.8 Gy	13	76.5%	16	94.1%
2.0 Gy	4	23.5%	1	5.9%
Dose to primary (BED_{10})				
~75 Gy	6	35.3%	8	47.1%
75~ Gy	11	64.7%	9	52.9%
Dose to gross LN (BED_{10})				
~72 Gy	6	35.3%	8	47.1%
72~ Gy	11	64.7%	7	41.2%
Dose to elective LN (BED_{10})				
~53 Gy	9	52.9%	10	58.8%
53~ Gy	8	47.1%	7	41.2%
Elective nodal coverage				
Ipsilat mediast LN only	1	5.9%	3	17.6%
Contralat mediast LN	12	70.6%	12	70.6%
Contralat hilar LN	3	17.6%	2	11.8%
Ipsilateral supraclav LN	9	52.9%	6	35.3%
Bilat supraclav LN	3	17.6%	2	11.8%

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Prophylactic cranial irradiation in non small cell lung cancer - should this be included in radical treatment

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Introduction: Brain metastases are three times less common in non-small cell lung cancers (NSCLC) compared to small cell lung cancer (SCLC).Patients with SCLC are offered prophylactic cranial irradiation (PCI) as part of radical treatment in limited stage disease. PCI is not routinely offered in NSCLC, however as the treatments for NSCLC improve, especially with new targeted therapy agents in conjunction with chemotherapy and radiotherapy we are finding that patients are increasingly relapsing in the brain. Therefore the beneficial role of prophylactic cranial irradiation in patients with NSCLC is questioned and is the subject of a number of on-going trials. We present a review of our experience at Guys and St. Thomas' Hospital to challenge this question.

Objective: A retrospective review of all patients with brain metastases from either small or non-small cell lung cancers over a period of six months to identify clinico-pathological markers that could categorize patients with NSCLC who would benefit from prophylactic cranial irradiation.

Methods: All patients with the diagnosis of lung cancer were identified on electronic patient records, via the lung cancer nurses and the radiotherapy department between May and October 2006. The data was then collected by extraction from the case notes. The main outcome measures were occurrence of brain metastases and whether it was dependent on the initial stage of the disease.

Results: The total number of patients found was 75, out of which those with non small cell lung cancer were 58 (77.3%) and those with small cell lung cancer were 17 (22.6%). In the non small cell lung cancer group 8 out of the total of 58 (13.79%) developed brain metastases